

**REMARKS**

Claims 1-13 and 23 were pending in the present application. By this Amendment, Applicants have amended claim 1 to address the Examiner's concerns. Support for the amendment to claim 1 can be found throughout the specification and claims as originally filed. Specifically, support can be found, *inter alia*, at page 1, line 38 to page 2, line 5. The present Amendment does not introduce any new matter and thus, its entry is respectfully requested. Upon entry of the present Amendment, claims 1-13, and 23, as amended, will remain pending and under examination.

**March 9, 2006 Office Action**

**Examiner's Claim Rejections Under 35 U.S.C. §112, second paragraph**

Claims 1-13 and 23 were rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. The Examiner pointed out that Claim 1 states a "medium which has a salt concentration of  $\leq 100$  mmol/L." The Examiner asserted, however, that it is unclear whether this is *total* salt concentration or the concentration of "any one of the component salts." The Examiner noted that the specification repeatedly refers to a "low sodium solution" (Pg. 2, Lines 7-10 and Pg. 10, Lines 28-32). The Examiner asserted that claims 2-13 and 23 are indefinite because they are dependent on Claim 1.

In response, without conceding the correctness of the Examiner's position, but to expedite allowance of the subject application, Applicants have amended claim 1 to recite that the salt concentration referred to therein is a total concentration. Applicants believe the claim was clear as written, in light of the disclosure throughout the specification that describes the claimed

method and its use of a "measurement medium" that has a salt concentration of  $\leq 100$  mmol/L. Nevertheless, to expedite allowance of the application, Applicants have amended the claim as noted. Applicants point out the disclosure at page 2, lines 2-5, noting that the concentration levels of the medium refer to "total concentration of the cations present in the medium." Applicants believe the amendment to claim 1 fully overcomes the Examiner's rejection, and thus, respectfully request reconsideration and withdrawal of the rejection of claims 1-13 and 23, under 35 U.S.C. §112, second paragraph.

Examiner's Claim Rejections Under 35 U.S.C. §103

The Examiner indicated that Applicants' arguments filed February 7, 2006, with respect to the rejection of claims 1-13 under 35 USC §103(a) have been fully considered and deemed persuasive. Therefore, the previous obviousness rejection has been withdrawn.

In response, Applicants acknowledge and appreciate the withdrawal of this rejection.

The Examiner has, however, set forth a new rejection of claims 1-13 and 23 under 35 U.S.C. §103, as allegedly obvious over Fromherz *et al.* (WO/2001/07002) in view of Meme *et al.* (2001).

According to the Examiner, Fromherz *et al.* teaches a method for determining whether a substance is a modulator of a membrane-associated voltage-controlled, ligand controlled, or mechanically controlled ion-channel/receptor system. (Pg. 3, Lines 47-50, Pg. 2, Lines 9-12). Moreover, the Examiner stated that Fromherz *et al.* teaches that the ion channel is a potassium channel hSlo (Pg. 2, Lines 47-48), that the ion-channel receptor system contains NMDA receptor (Pg. 3, Lines 1-2), that stimulation of the target component can be carried out via electrical, optical, or chemical means (Pg. 3, Lines 4-11), and that inherent characteristic of

voltage is that it is in either AC or DC form.

Furthermore, the Examiner asserted that Fromherz *et al.* teaches that the cell is in contact with an additional electrode, specifically a patch clamp (Pg. 5, Lines 20-22), that the potential sensitive electrode can be arranged on a chip, (Pg. 3, Line 16) and that a multiplicity of cells can be immobilized on a chip having a multiplicity of electrodes. (Pg. 5, Lines 18-19)

The Examiner acknowledged that Fromherz does not teach the use of a medium, which has a salt concentration of 100 Mmol/L or the use of an array comprising a multiplicity of cells immobilized on different electrodes for the purpose of testing a multiplicity of substances.

The Examiner asserted that Meme *et al.* teaches a method for determining whether a substance is a modulator of a target component in a cell, comprising the steps of:

Preparing a cell, containing a target component, wherein the cell is immobilized on a potential-sensitive electrode (Pg. 488, Column 1, Lines 31-41), bringing a substance to be tested in contact with the cell, in a medium which has a total salt concentration of < 100 mmol/L (Pg. 488, Column 2, Lines 14-22 and Pg. 492, Fig. 4), measuring the signal at the electrode due to the target component, and determining the effect of the substance to be tested on the measurement signal (Pg. 492, Fig. 4).

In the Examiner's view, it would have been obvious to combine the method of Fromherz, et al. for the determination of whether a substance is a modulator of a target component of a cell with the method as taught by Meme, et al. for determining whether a substance is a modulator of a target component of a cell wherein the method utilizes a medium which has a salt concentration of  $\leq 100$  mmol/L because, in the Examiner's opinion, the method of Meme, et al. showed a stronger and longer lasting response to a compound in the presence of a low salt solution. According to the Examiner, the ordinary artisan would have been motivated to apply the low salt solution of Meme, et al. to the method of Fromherz, et al. in order to test whether these effects would be found in alternate experimental situations. The Examiner asserted that the ordinary artisan would have had a reasonable expectation of success based upon the demonstrated success of Meme et al. in using a low salt solution in a similar method as described by Fromherz, et al.

The Examiner reiterated the position that Fromherz et al. teach the method of cultivating a multiplicity of cells immobilized on multiple electrodes. In the opinion expressed by the Examiner, it would have been obvious to the ordinary artisan at the time of the invention that if the technique were suitable for the testing of a single substance, then it would take only a little further modification to practice the technique using multiple substances. The ordinary artisan would have been motivated to do so, in the Examiner's view, because a method of screening multiple substances would be more efficient and cost effective than simply screening one at a time. Moreover, the Examiner asserted that the ordinary artisan would have had a reasonable expectation of success based on the previous success of the technique on testing a single substance.

In response, Applicants respectfully traverse the Examiner's rejection. The Meme publication, which is being cited now in combination with the previously cited Fromherz publication, describes that reduction of the sodium ion concentration in a medium leads to an increase of the calcium ion flux when the calcium flux in myocytes is measured. Applicants respectfully direct attention to page 488, right column, lines 14-22 and page 492, Figure 4.

In rejecting the claims, the Examiner has apparently taken the position that it was obvious on the basis of the results in Meme to employ a medium with a total salt concentration of  $\leq 100$  mmol/L in the method referred to in Fromherz, et al. Applicants respectfully disagree with the Examiner's conclusions. Meme teaches that the reduced sodium ion concentration is adjusted by adding equimolar amounts of N-methyl glucamine or lithium. Applicants point out, however, that both substances are cations, i.e., substances which must be included in the total salt concentration calculation. Thus, in Meme, the total salt concentration will not fall below 100mM even in solutions with a reduced sodium concentration. Accordingly, a combination of Fromherz and Meme does not lead one of ordinary skill in the art to the present invention. Meme does not reduce the total ion concentration, but rather replaces the sodium ions with different ion species. Therefore, the art cited by the Examiner does not teach the Applicants' claimed invention, and in particular, does not teach at least the feature that total ion concentration is reduced to 100mM or less. Therefore, Applicants' claimed invention is not rendered obvious by the art cited by the Examiner and thus, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1-13 and 23 under 35 U.S.C. §103.

In view of the above remarks and amendments, Applicants believe that all of the Examiner's rejections set forth in the March 9, 2006 Office Action have been fully overcome

and that the present application is in condition for allowance. The Examiner is invited to telephone the undersigned if it is deemed to expedite allowance of the application.

No fee is believed due in connection with the filing of this Amendment. If, however, any fee is deemed necessary, authorization is hereby given to charge such fee, or credit any overpayment, to Deposit Account No. 02-2135.

Respectfully submitted,

June 9, 2006

By

A handwritten signature in black ink, appearing to read 'P. Skacel', is written over a horizontal line.

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